REMARKS/ARGUMENTS

Claims 2-4, 7-13 and 16 are active.

Claim 2 has been amended for clarity as suggested in the Office Action at page 3. .

As described in the application, reacting a fructosyl peptide oxidase with the released fructosyl valine or fructosyl valylhistidine in the sample at a pH of 4.0 to 7.0 to produce hydrogen peroxide reduces the effect of fructosyl lysine compound in the assay. This is apparent from the claims as would be understood by one of ordinary skill in the art when read in light of the underlying specification. Accordingly, the rejection applied under 35 USC 112, second paragraph can be withdrawn.

The Examiner has raised a new rejection under 35 USC 102(e) citing to Hirokawa. For purposes of disclosure, Applicants note that Hirokawa published in the November 7, 2003 journal and apparently was available online as of October 9, 2003. Accordingly, Hirokawa is, contrary to the citation, applicable as prior art under 35 USC 102(b). Nonetheless, Applicants disagree with the Examiner's findings and conclusion that underlay the rejection. As apparent from the rejection at page 5 of the Action, the Examiner finds that Hirokawa treats a sample with a protease, reacts the resulting products with FPOX-E or -C and does so at a pH ranging from 6.5 to 8.

Hirokawa treats a sample (Fru-hexapeptide) with an *Aspergillys orzae* protease at a pH of 6.5 and thereafter adds a reaction mixture, including the oxidase, which is buffered at a pH of 8.0 (see page 106, col. 1 "*Enzymatic measurement of glycated peptide*"). Hirokawa describes specificity to Fru-ValHis and Fru-Val for these two oxidase (see page 108, col. 1). However, the reactions that Hirokawa describes on page 106, one at a pH of 6.5 and one at a pH of 8.0, do not support the derivation of a range of 6.5 to 8 as alleged in the rejection. That is, the pH of 6.5 is used in the protease treatment (10 microliter volume: 5 μl of standard solution and 5 μl of protease), which was subsequently heat-inactivated and then diluted with

the reaction mixture (140 μl) at a pH of 8.0. This combination of the two reactions, particularly where the reaction mixture constituted over 90% of the total reaction volume would have a pH very close, if not exactly, at 8.0 so when the oxidase is reacted with the released peptides, it would not be within the claimed range. Using these two separate reactions to derive a range as has been done in the rejection is not sustainable.

Indeed, Hirokawa teaches that the optimum pH of the reaction with FPOX-E and -C was between 7.5 and 8.0 and that a pH below 5.5 significantly impaired enzymatic activity (see page 107, col. 1: "*Properties of recombinant FPOX-E*"). Further, Hirokawa also describes optimum pH of the oxidase in reacting F-VH but in the absence of fructosyl lysine compounds, referencing Fig. 1, where Hirokawa conducted reactions in acetate and Mes-NaOH buffer at a pH between 4 and 7 (see open triangles and squares in FIG. 1 of Hirokawa). Thus, this disclosure does not describe or suggest the claimed invention in which the effects of fructosyl lysine compound is reduced by conducting that reaction at a pH as defined in the claims.

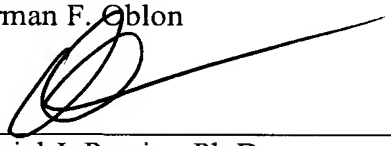
As explained previously, the present invention has solved the problem of the conventional assays by reacting the enzyme at a pH of 4.0 to 7.0 with fructosyl valine or fructosyl valylhistidine released from the glycated protein and by measuring the product of the reacting at a pH of 4.0 to 7.0. The present inventors have found that the reactivity of the enzyme for assaying glycated protein with fructosyl lysine is decreased under the pH condition thereby the adverse effect of a fructosyl lysine compound on measuring a glycated protein is reduced. Prior to the present invention, nobody has found the effect of pH condition on the reactivity of the enzyme to fructosyl lysine nor reported to modify pH condition in order to reduce the adverse effect of fructosyl lysine on the assay of glycated protein.

Therefore, the pH ranges coupled with the enzyme treatment for assaying fructosyl valine or fructosyl valylhistidine as defined in the claims reduce the effect a fructosyl lysine compound in assay of a glycated protein. Such is neither disclosed nor suggested by Hirokawa and as such withdrawal of the rejection is requested.

Upon consideration of the amendments and discussion submitted in this paper, a Notice of Allowance for all pending claims is also requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, L.L.P.
Norman F. Oblon



Daniel J. Pereira, Ph.D.
Attorney of Record
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/09)